

Oral Dextrose Gel in the Treatment of Neonatal Hypoglycemia:

An Evidence Based Practice Change

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Abstract

Neonatal hypoglycemia (NH) is a common concern among term and late preterm infants in the first day of life. Current NH management follows the American Academy of Pediatrics' guideline to treat with intravenous dextrose if blood sugar levels fall below a set threshold, which in many cases requires admission to the neonatal intensive care unit (NICU). Oral dextrose gel is currently an effective, inexpensive, and safe treatment for hypoglycemia in the pediatric and adult population, and researchers are exploring its use in the neonatal population. This prompted the following research question: in otherwise healthy late preterm and term newborns at risk for NH, how does the use of oral dextrose gel in addition to oral feedings, as compared to the current standard of care of oral feedings alone, affect blood sugar homeostasis in the first day of life? To answer this research question, upon completing a review of the literature and obtaining IRB approval on site, an evidence based practice change was implemented that included the addition of oral dextrose gel to the existing NH protocol in a tertiary hospital in the southwestern United States with a level III NICU and a busy delivery service.

Keywords: neonatal hypoglycemia treatment, neonatal hypoglycemia oral dextrose gel, neonatal blood glucose homeostasis, neonatal hypoglycemia management, neonatal glucose metabolism, oral dextrose gel versus intravenous dextrose, neonatal hypoglycemia protocol

Oral Dextrose Gel in the Treatment of Neonatal Hypoglycemia

Neonatal hypoglycemia (NH) is a common problem in the newborn period that usually resolves on its own in the first few days of life. Not all infants who have low blood sugar levels are symptomatic; therefore many hospitals have NH protocols that screen infants based on risk factors. Infants with critically low blood glucose levels defined as $<30\text{mg/dL}$, if left untreated for a prolonged period of time, can have significantly impaired motor and mental development at 18 months of age, although current research has yet to determine the blood glucose level and duration threshold at which this irreversible damage occurs.

Background & Significance

Neonatal hypoglycemia is the leading cause for NICU admissions among late preterm and term infants (Bennett, Headtke, & Rowe-Telow, 2015). It is commonly seen in otherwise healthy newborns by one to two hours of life, and is often asymptomatic and transient with blood glucose levels as low as 30mg/dL . While NH is considered a normal part of transition to extra-uterine life that usually resolves by the first day of life, in some infants blood glucose homeostasis takes longer regardless of the infant being asymptomatic and feeding well.

Historically, treatment has followed the American Academy of Pediatrics' (AAP) recommendation to feed the infant and recheck blood glucose in one hour (Committee on Fetus and Newborn & Adamkin, 2011). If the repeat blood glucose is less than 25mg/dL despite oral feeding, the infant will require treatment with IV dextrose, which means that the infant will be admitted to the NICU for treatment. Not only does this separation interfere with maternal-infant interaction in the first day of life, it can also lead to decreased breastfeeding rates (Bennett et al., 2015). Many existing hospital NH protocols specify blood glucose screening procedures, and if after a specified amount of time the infant's blood glucose remains out of range despite feeding

well and being asymptomatic, the AAP recommends IV dextrose administration even though a blood glucose level of 45mg/dL on the first day of life is not nearly as significant for neurological damage as on the third day of life, where the blood sugar levels should be greater than 70mg/dL on average (Brown & Rozance, 2016).

Problem Statement

Persistent NH, when left untreated, has been linked to poor neurological outcomes such as seizures, learning deficits, cerebral palsy and mental retardation (Bennett, Fagan, Chaharbakhshi, Zamfirova, & Flicker, 2016). It is estimated that 15% of otherwise healthy newborns are affected by neonatal hypoglycemia (Mosalli, 2014). Certain factors place newborn infants at a higher risk of developing hypoglycemia in the first day of life, and those risk factors include being born to a diabetic mother (IDM), late prematurity (34-37 weeks gestation), post maturity (> 41 weeks gestation), small for gestational age (less than the 10th percentile in weight for gestational age), large for gestational age (greater than the 90th percentile in weight for gestational age), and other reasons after birth such as poor feeding (Harris, Weston, & Harding, 2012).

According to the March of Dimes Perinatal Data Center (2011), 19% of special care nursery (SCN) or neonatal intensive care (NICU) admissions were late preterm infants (34-37 weeks gestation) with hospital length of stay (LOS) ranging from 5.9 to 9.8 days. Nearly six percent of late preterm infants admitted to SCN or NICU units had the admitting diagnosis of NH, and no other complications that required them to be in the NICU for treatment. In the facility where this evidence based practice change was implemented, 49 infants who were otherwise healthy were admitted to the NICU for NH treatment in 2017 alone.

It is estimated that the hospital cost for a NICU stay for NH for an otherwise healthy late preterm or term infant can range from \$37,137 to \$51,083 (March of Dimes Perinatal Data Center, 2011). A regular newborn nursery admission for a healthy late preterm or term newborn is estimated to be only \$4415 (Rawat et al., 2016). In the facility where this evidence based practice change was implemented, the cost of caring for these 49 infants who were otherwise healthy could be estimated to be around 2.5 million dollars in 2017. This prompted the following PICOT question: in otherwise healthy late preterm and term newborns at risk for NH, how does the use of oral dextrose gel in addition to oral feedings, as compared to the current standard of care of oral feedings alone, affect blood sugar homeostasis in the first day of life?

Search Strategy

In order to answer the aforementioned PICOT question, the following databases were searched: The Cochrane Library, PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), and ASU Libraries OneSearch. Keywords included: *neonatal hypoglycemia, neonatal hypoglycaemia, neonatal hypoglycemia treatment, neonatal hypoglycemia oral dextrose gel, neonatal blood glucose homeostasis, neonatal hypoglycemia management, neonatal glucose metabolism, oral dextrose gel versus intravenous dextrose, neonatal hypoglycemia protocol*. Both American and English spellings of keywords were used. Filters were set to include research articles with publication dates within the last five years. The strategy also included ancestral searching and reviews of gray literature to determine the overall incidence of NH and to identify differences in NH incidence related to different risk factors, in addition to different treatment strategies for NH.

The initial search for “neonatal hypoglycaemia” in the Cochrane Library yielded 196 articles. When the search was limited to “neonatal hypoglycaemia AND treatment”, the results

were narrowed down to 159 articles. A further limitation to only include “neonatal hypoglycaemia AND dextrose gel” resulted in 16 articles. After close examination, only one systematic review in the Cochrane Library was applicable to this project’s topic and retained for further review (Appendix A).

PubMed was searched using the keywords “neonatal hypoglycemia management”, which resulted in 714 possible articles. After adding additional limits to only include articles from the most recent five years and peer-reviewed articles, while changing the search terms to “neonatal hypoglycemia oral dextrose gel” the search yielded seven articles, all of which were retained for further review (Appendix B).

A search using CINAHL using the key words “neonatal hypoglycemia treatment” yielded 11 results that were published within the past five years. After adding additional filters for peer reviewed articles and research, one article remained. A separate CINAHL keyword search using “neonatal hypoglycemia oral dextrose gel” yielded two articles, and both were retained for review (Appendix C).

Lastly, ASULibraries OneSearch was used with the following keywords “neonatal hypoglycemia oral dextrose”. Limitations that were added were publication date within past five years and scholarly and peer-reviewed journal articles. This yielded 146 articles, however, the majority of the articles focused on gestational diabetes and implications for pregnant women rather than hypoglycemia in the neonatal population (Appendix D).

Eleven final articles were selected for critical appraisal: one systematic review, six randomized controlled trials, and four retrospective chart reviews.

Evidence Synthesis

While a review of the literature confirms that there is no specific plasma glucose concentration or duration of NH that can predict permanent neurological injury in at risk infants, the treatment for asymptomatic hypoglycemic newborns in the first day of life is up for debate (Committee on Fetus and Newborn & Adamkin, 2011). Until recently, NH has been treated by IV dextrose administration as recommended by the AAP (Bennett et al., 2016), but recent literature reviews show that oral dextrose gel is being investigated as a possible alternative treatment for NH.

A retrospective chart review pre- and post-implementation of oral dextrose gel in an NH treatment trial found that the primary admitting diagnosis to the NICU for NH decreased from a mean of 11% to 2% (Bennett et al., 2015). In a follow up study led by Bennett et al. (2016), the researchers found that using oral dextrose gel in addition to oral feeding reduced NICU admissions significantly for otherwise healthy newborns with transient NH. During a 14-month period, they noted a continued decrease in NICU admissions for NH among late preterm and term infants (Bennett et al., 2016).

Brown and Rozance (2016) noted that while in their study oral dextrose gel appeared to be effective in treating NH in asymptomatic term infants, they felt the same results likely would not apply to infants with symptomatic or severe NH. Their concern was that using oral dextrose gel in symptomatic infants might delay treatment with IV dextrose and lead to irreversible neurological damage (Brown & Rozance, 2016).

Harding et al. (2015) designed a randomized, placebo controlled trial that proposed the prevention of NH by giving oral dextrose gel to infants who are at risk for NH but are not currently experiencing low blood sugar levels. In a follow up study led by Hegarty et al. (2016),

prophylactic use of oral dextrose gel in at risk newborns resulted in fewer NICU admissions for NH compared to the placebo group.

The Sugar Babies Study, a randomized, double blind, placebo-controlled trial done in New Zealand, found that the addition of oral dextrose gel to oral feeding reduced the frequency of NH treatment failure leading to NICU admission for IV dextrose administration, as compared with placebo (Harris et al., 2013).

Another study found that 51% of term and late preterm infants who were considered to be at risk for developing NH in the first day of life became hypoglycemic, with 19% developing severe NH (Harris, Weston, & Harding, 2012). While this particular study did not discuss the use of oral dextrose gel as a possible non-invasive and alternative treatment for NH, the findings did underline the importance of routine screening protocols for at risk infants, as these infants are at significantly higher risk for developing NH especially when multiple risk factors are present. Harris et al. (2012) then used the findings of this study in subsequent research that specifically looked at the use of oral dextrose gel in NH treatment and prevention.

A Cochrane review led by Weston et al. (2016) found that the use of 40% oral dextrose gel reduced NICU admissions for NH and also reduced the frequency of mother-baby separation for NH treatment. The Cochrane review found no evidence of adverse effects of oral dextrose use during the neonatal period or at two years of age (Weston et al., 2016).

Mosalli (2014) found that at risk infants treated with oral dextrose gel were nearly twice as likely to achieve blood glucose homeostasis without needing additional interventions such as IV dextrose, as compared to their counterparts who received a placebo gel.

Another study led by Rawat et al. (2016) found that oral dextrose gel increased blood glucose levels in 74% of their study group, which led to reduced NICU admissions for IV

dextrose treatment. They also noted that exclusive breastfeeding rates improved from 19% to 28% (Rawat et al., 2016).

While the use of oral dextrose gel may be an innovative and inexpensive solution to a long existing problem in the NICU, it is also important to note that there should be specific guidelines in place by what measure NH is diagnosed. Ly, Alexander, Akinmboni, Woo, and Driscoll (2016) set out to improve the diagnosis of NH by comparing point of care glucose (POCG) measurements with serum glucose measurements. What they found was that POCG measurements can vary greatly in accuracy, especially if blood glucose levels are below normal. If NH is suspected after a low POCG measurement, a confirmatory serum glucose test needs to be done to prevent delay in treatment (Ly et al., 2016). While the researchers could not determine a blood glucose threshold that would warrant immediate treatment besides oral feeding for an asymptomatic hypoglycemic newborn as the normal physiologic nadir is suspected to be around 30mg/dL, many hospital policies follow the AAP's guideline to intervene at a blood glucose level <40mg/dL (Ly et al., 2016).

Recent studies are pointing towards oral dextrose gel being a safe, inexpensive, and non-invasive alternative to the traditional IV dextrose treatment for NH for late preterm and term infants who otherwise have no other health concerns that would require treatment in the NICU. If indeed effective in helping achieve blood glucose homeostasis in the first day of life, not only could the inclusion of oral dextrose gel in existing NH policies potentially reduce unnecessary NICU admissions, it could also improve exclusive breastfeeding rates which is a Joint Commission perinatal core measure.

Purpose Statement

The purpose of this evidence based practice change is to add oral dextrose gel to the existing NH protocol as a safe, effective, and alternative treatment for NH, as compared to the previous standard of care in this particular setting where infants were admitted to the NICU to receive treatment with IV dextrose if oral feedings alone were not effective at achieving blood glucose homeostasis within a set time frame. This practice change will benefit the hospital by reducing healthcare costs associated with NICU admissions, and will also benefit infants and their families by shortening their hospital length of stay and therefore reduce associated healthcare expenses and by not separating the mother-infant dyad.

Evidence Based Practice Model

The model chosen to guide the application of the synthesized evidence is the Model for Evidence-Based Practice Change (Rosswurm & Larrabee, 1999). This model illustrates the process for implementing research evidence into clinical practice in six specific steps (Appendix E). The first step is identification of a clinical issue, collecting internal and external data, and involving stakeholders. Research evidence supporting the proposed practice change was presented to the nursing research council, pediatricians, neonatologists, neonatal nurse practitioners, and hospital leadership.

The second step is to do a literature search to locate the best evidence. Step three is to critically analyze the evidence found in step two. The fourth step is to define practice change, and design a protocol. Using data from the literature search, an updated NH protocol was created that included an NH algorithm that outlined the steps nurses would take to identify infants at risk for NH and when to administer oral dextrose gel and the frequency of blood glucose checks.

The fifth step is implementation of the new protocol and evaluating the study. Evaluation of the study included comparing data of 27 infants post-implementation of the practice change who met risk factors for NH to 27 infants pre-implementation of the practice change. Care was taken to ensure that both groups had similar birth weights, gestational ages, risk factors, and initial blood glucose values to ensure a homogenous sample. Collecting data from a controlled setting such as one hospital will help determine the effectiveness of the evidence-based protocol, and using this model will allow for either modification or implementation of a practice protocol (Melnik & Fineout-Overholt, 2015). Once the fifth step is finalized and conclusions and recommendations have been made, the final step is to maintain the change in practice, and to implement the change at other hospitals in the same system.

Theoretical Model

The theoretical model that guided this project was Lewin's Theory of Planned Change. Lewin's change theory describes the process of effectively implementing change as a simple three-step process. Using Lewin's Theory of Planned Change, the first step is identifying a problem (Shirey, 2013). The problem of NH treatment was identified and staff who would be taking care of infants that would qualify to receive oral dextrose gel were included in education about the practice change. This ensured staff readiness for the change.

The second stage of Lewin's change theory looks at change as a process rather than an event (Shirey, 2013). In cooperation with hospital educators, the researcher ensured that staff was ready for the change, had a protocol in place, and implemented the practice change.

The third and last stage of Lewin's theory is refreezing the change (Shirey, 2013). What this entails is ensuring that the change is sustained to continually improve outcomes. This was achieved by keeping communication lines open with the education department and staff, to

ensure that if there were any concerns they would be able to voice those concerns freely to ensure staff support throughout the practice change. Upon completion of this project, the results will be shared with the hospital staff and nursing research committee.

Project Methods

Human subjects protection was obtained by the researcher from the hospital and university IRB prior to implementing the practice change. The researcher created an updated NH protocol along with an NH algorithm (Appendix F) that was displayed in multiple areas for easy reference. Nursing education was delivered via a voice-over PowerPoint created by the researcher and approved by the hospital nursing research committee to ensure consistency in the delivery of educational materials. This PowerPoint remains available on the hospital's intranet and nurses providing care for infants in labor and delivery, newborn nursery, postpartum, and NICU were all educated on the use of the new algorithm. Questions regarding the new protocol were answered by the researcher directly to ensure consistency. Instruments used to obtain blood glucose levels were bedside glucometers that were maintained by the hospital laboratory staff following manufacturer recommendation, and nursing staff performed quality control tests daily. Data collection included chart reviews of 27 infants with similar inclusion criteria who received IV dextrose as treatment for NH in the previous year, and 27 infants post-implementation of the new protocol who met risk factors and/or received oral dextrose gel as initial treatment for NH. All statistical analysis was performed using SPSS v.24 (IBM Corp, 2016).

Project Results

Upon data collection of 54 infants with similar demographical information, statistical analysis was performed to determine that this was a homogenous sample. While the gestational age range for this project included infants born at 34 weeks to greater than 41 weeks, both the

pre-implementation group and post-implementation group had similar gestational age means, $37\frac{2}{7}$ (SD=1.8) and $37\frac{5}{7}$ (SD=2) respectively. Additionally, birth weights in both groups ranged from 1630 gram to 5060 gram, with the mean birth weight in the pre-implementation group at 3392 gram (SD=892) and in the post-implementation group 3056 gram (SD=697). Using a t-test, no statistically significant differences were identified between both groups' demographics.

While none of the infants in the pre-implementation group received oral dextrose gel for NH treatment, all 27 infants in this group received IV dextrose infusion as treatment at a standard rate of 200mg/kg which is identical to the oral dextrose gel dose of 200mg/kg. Because the infants in this group all received IV dextrose this group has a 100% NICU admission rate. In the post-implementation group, 24 out of 27 infants received oral dextrose gel. While seven infants in the post-implementation group were admitted to the NICU for NH, chart reviews revealed that only two of those infants were admitted for NH and not other diagnoses that required admission to the NICU. This means that in the post-implementation group, the NICU admission rate for NH is 9% with a $p < 0.001$ which indicates statistical significance.

The clinical significance of the two infants who received oral dextrose gel and were admitted to the NICU for treatment with IV dextrose is that they likely experienced refractory hypoglycemia secondary to being IDM, suggesting the possibility of hyperinsulinism, which complicates NH.

Discussion

Upon data analysis, results will be presented to the nursing research committee to be shared with nursing staff. This project will be sustained in the hospital as it is evidence based practice, but slight modifications to the protocol will be made based on the results of this study, such as changing the post term age ranges to greater than 42 weeks (currently set at >41 weeks).

Conclusion

In the current hospital setting, the use of oral dextrose gel in addition to oral feedings was superior to treating NH as compared to oral feedings alone. The protocol created will be shared with other facilities, and larger studies need to be done to see if results are generalizable. Additionally, more research needs to be done to include small community or outlying hospitals that do not have NICUs, to see if the incorporation of oral dextrose gel in their existing NH protocols in newborn nurseries can also decrease the need for patient transfer to other hospitals for higher level of care in this particular population.

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Appendix A

Search Strategy 1: Cochrane Library

Wiley Online Library

 **Cochrane Library** Trusted evidence. Informed decisions. Better health. [Log in / Register](#)

Search Search Manager Medical Terms (MeSH) Browse

To search an exact word(s) use quotation marks, e.g. "hospital" finds hospital; hospital (no quotation marks) finds hospital and hospitals; pay finds paid, pays, paying, payed)

[Add to top](#)

−	+	#1	neonatal hypoglycemia dextrose gel:ti,ab,kw (Word variations have been searched)	S	14
−	Edit	+	#2	neonatal hypoglycaemia	196
−	Edit	+	#3	neonatal hypoglycaemia treatment	159
−	Edit	+	#4	neonatal hypoglycaemia dextrose gel	16
−	Edit	+	#5	neonatal blood glucose homeostasis	43
−	+	#6			N/A

[Clear Strategy](#) [Search Help](#) ☐ Highlight orphan lines

Save strategy

Strategy Name [Save Strategy](#)

Appendix B

Search Strategy 2: PubMed

NCBI Resources How To Sign in to NCBI

PubMed Home More Resources Help

PubMed Advanced Search Builder

[YouTube Tutorial](#)

Use the builder below to create your search

[Edit](#) [Clear](#)

Builder

All Fields [Show index list](#)

AND All Fields [Show index list](#)

[Search](#) or [Add to history](#)

History [Download history](#) [Clear history](#)

Search	Add to builder	Query	Items found	Time
#7	Add	Search neonatal glucose metabolism	9139	17:58:26
#4	Add	Search neonatal hypoglycemia protocol	74	17:54:53
#3	Add	Search oral dextrose gel versus intravenous dextrose	2	17:54:37
#2	Add	Search neonatal hypoglycemia oral dextrose gel	7	17:54:09
#1	Add	Search neonatal hypoglycaemia management	714	17:53:50

Appendix C

Search Strategy 3: EBSCOhost CINAHLplus with full text

EBSCOhost Searching: CINAHL Plus with Full Text [Choose Databases](#)
☐ Suggest Subject Terms

Select a Field (option... [Search](#) [Clear](#) [?](#)

AND Select a Field (option... [+](#) [-](#)

AND Select a Field (option... [+](#) [-](#)

[Basic Search](#) [Advanced Search](#) [Search History](#)

Search History/Alerts

[Print Search History](#) | [Retrieve Searches](#) | [Retrieve Alerts](#) | [Save Searches / Alerts](#)

☐ Select / deselect all [Search with AND](#) [Search with OR](#) [Delete Searches](#) [Refresh Search Results](#)

	Search ID#	Search Terms	Search Options	Actions
<input type="checkbox"/>	S4	define neonatal hypoglycemia	Search modes - Boolean/Phrase	View Results (1) View Details Edit
<input type="checkbox"/>	S3	neonatal hypoglycemia oral dextrose gel	Search modes - Boolean/Phrase	View Results (2) View Details Edit
<input type="checkbox"/>	S2	neonatal hypoglycemia treatment	Limiters - Published Date: 20120101-20171231; Peer Reviewed; Publication Type: Research Search modes - Boolean/Phrase	View Results (1) View Details Edit
<input type="checkbox"/>	S1	neonatal hypoglycemia treatment	Search modes - Boolean/Phrase	View Results (11) View Details Edit

Refine Results

Current Search [v](#)

Search Results: 1 - 2 of 2



Relevance [v](#) Page Options [v](#) [Share](#) [v](#) [Plum Print](#) [v](#)

1. Randomised trial of neonatal hypoglycaemia prevention with oral dextrose gel (hPOD):

Appendix D

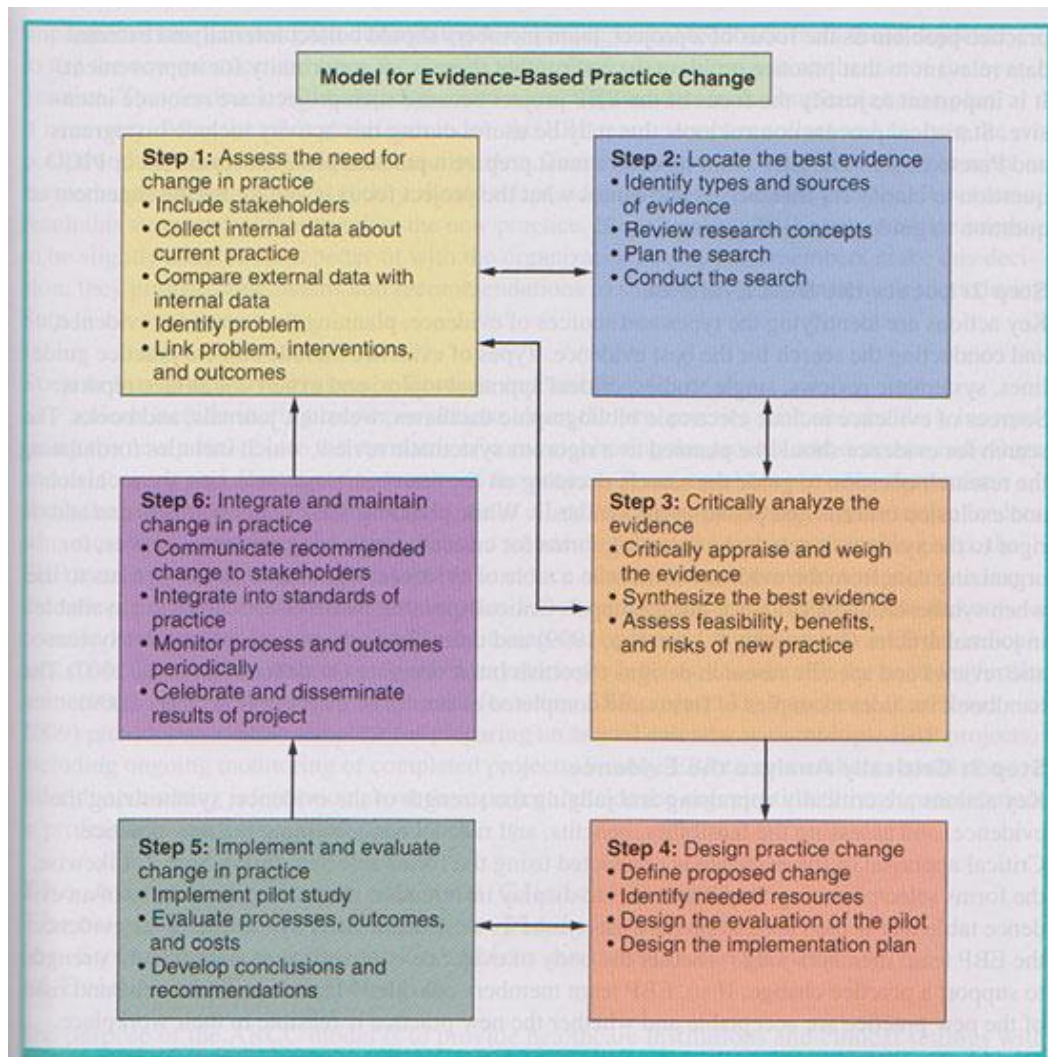
Search Strategy 4: ASU Libraries OneSearch

The screenshot shows the ASU Libraries OneSearch interface. The search bar at the top contains the query "(neonatal hypoglycemia oral dextrose gel)". The left sidebar offers filters for "REFINE YOUR SEARCH" (Full Text Online, Scholarly & Peer-Review, Library Catalog) and "CONTENT TYPE" (Journal Article, Book Review, Trade Publication Article, Conference Proceeding, Magazine Article, More...). The "DISCIPLINE" filter lists medicine (501), anatomy & physiology (39), biology (33), nursing (25), and veterinary medicine (22). The main results area, titled "Database Recommendations", lists two items:

- 1**  **Use of Dextrose Gel Reverses Neonatal Hypoglycemia and Decreases Admissions to the NICU**
by [Bennett, Catherine](#); [Headtkie, Elyse](#); [Rowe-Telow, Meg](#)
Journal of Obstetric, Gynecologic, & Neonatal Nursing, 06/2015, Volume 44, Issue s1
... Poster Presentation Objective To reduce newborn admission to the **neonatal** intensive care unit (NICU) for the diagnosis of **neonatal hypoglycemia** by using 40...
Journal Article: [Full Text Online](#)
[Preview](#)
- 2**  **Randomised trial of neonatal hypoglycaemia prevention with oral dextrose gel (hPOD): study protocol**
by [Harding, Jane E](#); [Hegarty, Joanne E](#); [Crowther, Caroline A](#); [More...](#)
BMC pediatrics, 2015, Volume 15, Issue 1
.... Treatment of hypoglycaemia usually involves additional feeding,

Appendix E

Model for Evidence-Based Practice Change (Rosswurm & Larrabee, 1999)



Appendix F

Neonatal Hypoglycemia Algorithm

